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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/085,117	02/27/2002	David W. Morris	PP23697.0001/20366-005001	7176

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Novartis Vaccines and Diagnostics, Inc.  
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EXAMINER
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AEDER, SEAN E

ART UNIT	PAPER NUMBER
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1642

MAIL DATE	DELIVERY MODE
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07/08/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>		<b>Applicant(s)</b>	
	10/085,117		MORRIS ET AL.	
	<b>Examiner</b>		<b>Art Unit</b>	
	SEAN E. AEDER		1642	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 26 March 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 24,26,27,29 and 37-39 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 24,26,27,29 and 37-39 is/are rejected.
- 7) ☒ Claim(s) 38 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

***Detailed Action***

The Amendments and Remarks filed 3/26/08 in response to the Office Action of 11/16/07 are acknowledged and have been entered.

Claims 38-39 have been added by Applicant.

Claims 24, 26, 27, 29, and 37-39 are pending.

Claims 24, 26, 27, 29, and 37 have been amended by Applicant.

Claims 24, 26, 27, 29, and 37-39 are currently under examination.

The following Office Action contains NEW GROUNDS of rejections necessitated by amendments.

***Objections Withdrawn***

The objections to claims 24 and 37 are withdrawn.

***Rejections Withdrawn***

The previous rejections under 35 U.S.C. 112 first paragraph, for reciting New Matter, have been withdrawn.

***New Objections***

Claim 38 is objected to because of an apparent typographical error. Claim 38 recites: "A method of colon cancer comprising...". There appears to be a word missing between "cancer" and "comprising". It is suspected Applicant intended claim 38 to

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recite: "A method of colon cancer diagnosis comprising...". Proper correction is required.

***New Rejections Necessitated by Amendments***

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 38 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 38 is rejected as indefinite for reciting "highly" stringent hybridization conditions, as the specification does not distinctly define the limitations of such conditions. For example, the specification teaches exemplary stringent conditions include hybridization at 60C in a solution with a sodium ion concentration from about 0.01 to 1.0M, pH 7.0 to 8.3 comprising formamide (page 11, in particular). However, those conditions are not *defined* by the claims and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. This rejection can be obviated by distinctly defining the conditions, **including washing conditions**, under which highly stringent conditions are practiced.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

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art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24, 26, 27, 29, and 37-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. See also *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

The claims are broadly drawn to *contradictory* methods wherein a decrease of at least 50% in a level of expression of a nucleic acid (including nucleic acids comprising SEQ ID NO:167, full complements of SEQ ID NO:167, and *just any nucleic acid the hybridizes under highly stringent conditions to SEQ ID NO:167 or the complete complement thereof*) between a patient sample and a second sample indicates the

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patient has colon cancer. The claims do not point-out whether lower levels of said nucleic acid are found in samples of a patient that is to be diagnosed as having colon cancer as compared to levels of said nucleic acid in control samples or whether the lower levels of said nucleic acids are found in the control samples as compared to a patient that is to be diagnosed as having colon cancer. Therefore, the claims are broadly drawn to contradictory methods wherein patients with lower levels of said nucleic acid and patients with higher levels of said nucleic acid, as compared to levels of said nucleic acid in negative controls, are diagnosed with colon cancer.

The specification discloses that SEQ ID NO:167 is a cancer associated (CA) nucleic acid (page 10 lines 9-12 and table 1, in particular). The specification further discloses that CA nucleic acids are nucleic acids that were identified through use of oncogenic retroviruses, whose sequences insert into the genome of lymphatic tissue resulting in carcinoma (page 3 lines 17-29 and page 7 lines 20-24, in particular). The specification further discloses that CA nucleic acids can be downregulated in carcinomas *and* discloses that CA nucleic acids can be upregulated in carcinomas (see lines 29-38 on page 7, in particular). *However*, of the hundreds of CA nucleic acids disclosed in the specification (see Table 1), the specification does not disclose which CA nucleic acids are upregulated and which are downregulated in particular carcinomas. Further, the specification lacks working examples demonstrating contradictory methods wherein patients with lower levels of said nucleic acid and patients with higher levels of said nucleic acid, as compared to levels of said nucleic acid in negative controls, are diagnosed with colon cancer.

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The level of unpredictability for the detection of any disease is quite high. The state of the prior art dictates that if a particular expression level of a molecule such as a polynucleotide comprising the sequence set forth as SEQ ID NO:167 is to be used as a surrogate for a particular diseased state, said particular expression level must be demonstrated with said particular diseased state. There must be some expression pattern that would allow the particular expression level of the molecule to be used to indicate said particular diseased state. For example, Tockman et al (Cancer Res., 1992, 52:2711s-2718s) teach considerations necessary in bringing a cancer biomarker (intermediate end point marker) to successful application. Tockman et al teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials (see abstract). Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials (p. 2716s, col 2). Therefore, absent evidence of a particular expression pattern of a molecule including the correlation to a particular diseased state, one of skill in the art is not enabled to use said particular expression pattern as an indication of said particular diseased state without undue experimentation.

Since neither the specification nor the prior art provide evidence of contradictory methods wherein patients with lower levels of nucleic acids comprising SEQ ID NO:167, full complements of SEQ ID NO:167, or just any nucleic acid the hybridizes under highly

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stringent conditions to SEQ ID NO:167 or the complete complement thereof and patients with higher levels of said nucleic acids, as compared to levels of said nucleic acids in negative controls, are diagnosed with colon cancer, a practitioner wishing to practice the claimed invention would be required to provide extensive experimentation to demonstrate such an association. Such experimentation would in itself be inventive.

In view of the teachings above and the lack of guidance, workable examples and or exemplification in the specification, it would require undue experimentation by one of skill in the art to determine with any predictability, that the method would function as claimed.

### ***Summary***

No claim is allowed.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

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extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SEAN E. AEDER whose telephone number is (571)272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MISOOK YU/  
Primary Examiner, Art Unit 1642

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